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Dietary magnesium intake is related to metabolic syndrome in older Americans

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W. Juan Center for Nutrition Policy and Promotion USDA Arlington (VA), USA ■ **Abstract** Background Magnesium (Mg) is an essential cofactor for enzymes involved in glucose and insulin metabolism. Low intakes of dietary magnesium may be linked to greater risk of metabolic syndrome (MS) in older adults. Aim of the study The objective of this study was to examine the cross-sectional relationship between dietary Mg intake, metabolic risk factors and MS in elderly adults. Methods This study was conducted in a sample of 535 (179 men and 356 women) community-living adults aged 60 years and in Boston Massachusetts between the years 1981 and 1984. Dietary Mg intake was assessed by a 3-day food record and categorized by quartiles of dietary intake. The MS was defined based on criteria set by the Third Report of the National Cholesterol Education Program except that body mass index was used in place of waist circumference. Logistic regression analysis was used to examine the association between quartile categories of Mg intake, prevalence of MS and components of the MS. Models

were adjusted for age, gender, BMI, race, educational attainment, marital status, smoking status, alcohol intake, exercise, energy intake, percentage of calories from saturated fat, use of antihypertensive or lipid medication. Results Mg intake was inversely associated with the MS; those with the highest intake of Mg had significantly lower risk of having MS compared to the lowest quartile of intake (OR: 0.36, 95% CI 0.19-0.69, P for trend 0.002). Significant inverse relationships were observed between Mg intake and BMI (OR: 0.47, 95% CI: 0.22-1.00, P trend = 0.03), and fasting glucose (OR: 0.41, 95% CI 0.22-0.77, P trend = 0.005). Conclusion Our study demonstrates that Mg intake is inversely associated with prevalence of the MS in older adults. Older adults should be encouraged to eat foods rich in Mg, such as green vegetables, legumes and whole-grains.

■ **Key words** dietary magnesium – metabolic syndrome – older adults

Introduction

Metabolic Syndrome (MS) is a condition characterized by a clustering of several risk factors including,

abdominal adiposity, dyslipidemia, glucose intolerance and hypertension [19]. In the US, over 40% of people older than 60 years have the MS [7], predisposing more individuals to type 2 diabetes mellitus (DM) and cardiovascular disease risk. Older individ-

uals, particularly those who are not taking a dietary supplement, may not be consuming adequate dietary magnesium in their diets [8]. Data from the 1999 to 2000 National Health and Nutrition Examination Survey (NHANES) showed that the average magnesium intake was 239 mg in women and 350 mg in men [8], below the sex-specific recommended dietary allowance of 320 mg for women and 420 mg for men [13]. In terms of population growth, older adults (≥65 years) represent the fastest-growing segment of the US population [12] and therefore potential dietary interventions that may prevent the progression of the MS may have substantial health impacts.

Magnesium (Mg) is an essential cofactor for enzymes involved in glucose and insulin metabolism [17, 24]. In patients with type 2 DM who had low magnesium levels, randomization to an oral magnesium supplementation improved insulin sensitivity and glucose control after 16 weeks [20]. Other randomized studies have found that Mg supplementation improves insulin sensitivity in both healthy older adults [17] and patients with type 2 DM [16]. Based on the data from nine prospective studies that examined the relationship between dietary magnesium intake and type 2 DM risk, a recent metaanalysis reported that risk was 33% lower among those with the highest compared to the lowest magnesium intake [25]. Furthermore, both low Mg intake and low Mg status have been associated with a higher prevalence of the MS [4, 10, 11, 28]. To date, most studies have used a food frequency questionnaire to rank individuals according to reported magnesium intake in younger populations [11, 28]. The relationship between dietary Mg intake (in this case derived from diet records) and risk of MS has not yet been examined in older individuals (>60 years of age). One advantage to using a food record to capture diet in older adults is that it is not reliant on memory because all foods and beverages are recorded at the time of consumption. The purpose of this study was to examine whether Mg intake was related to metabolic risk factors and prevalence of the MS in older adults. Our hypothesis was that greater Mg intake was favorably associated with metabolic risk factors and a lower prevalence of the MS.

Subjects and methods

Subjects

This study, conducted in Boston, Massachusetts (1981–1984), collected nutrition information on 747 community-living individuals aged 60 years and over. Of the 747 subjects who participated in the study, 126 individuals were excluded from the analysis due to

incomplete food records. Additionally, excluded from the analysis, were the data of individuals taking insulin or oral glycemic agents (n=39), missing information on body weight (n=24), biochemistry (n=15), smoking and exercise (n=8), reducing the final sample to 535 subjects. All study procedures were approved by the Institutional Review Board at Tufts Medical Center. All participants provided signed informed consent prior to entry into the study.

Dietary intake

A dietitian instructed the subjects on how to keep a consecutive 3-d food record starting the day after the instructions were provided. Upon completion, the food records were reviewed by the dietitian for accuracy and completeness. Foods were coded for magnesium using the USDA Food and Nutrient Database for Dietary Studies (Version 1.0). Total Mg intake represents the sum of Mg intake from both supplements and dietary sources.

Examination and interview

A trained nurse practitioner obtained heights and weights from study participants. Each study participant was weighed in light indoor clothing on a calibrated portable bathroom scale. Heights were measured using a tape measure pasted on the wall. Body mass index (BMI) was calculated as weight (kg)/height (m)². The nurse practitioner measured each individual's blood pressure and obtained a medical history and detailed information on medication and nutrient supplement use. Additional information was obtained on demographic characteristics, health practices and eating habits such as gender, race, marital status, educational attainment, living arrangement, exercise, beverage and alcohol consumption and tobacco use.

After an overnight fast of 10–12 h, a venous blood sample was drawn to measure fasting concentrations of total and HDL cholesterol, triacylglycerol, and glucose. Plasma total cholesterol and HDL were measured by enzymatic spectrophotometry, with isolation of HDL from magnesium/phosphotungstate serum supernate [1, 14]. Plasma triglyceride level was measured by enzymatic spectrophotometry using ammonium ions and acetyl acetone [9]. Serum glucose concentration was measured by enzymatic spectrophotometry analysis using the procedure by Barthelmai and Czok [2].

With the exception of abdominal adiposity, MS risk factors were defined in accordance with ATP III criteria [5]. The MS criteria were defined as follows: hypertriglyceridaemia: serum triglycerides ≥150 mg/dl

(1.7 mmol/l); low HDL cholesterol <40 mg/dl (1.1 mmol/l) in men and <50 mg/dl (1.3 mmol) in women; elevated blood pressure ≥130/85 mmHg or receiving blood pressure medication; we used the revised lower criterion for fasting glucose of 100 mg/dl rather than 110 mg/dl [6]. In this study, measurements of waist circumference were not taken on study participants and thus we used a BMI ≥31 kg/m² for men and ≥27 kg/m² for women to capture abdominal adiposity, based on corresponding waist circumference thresholds in a representative population [30]. Metabolic syndrome was defined as having three or more of the five metabolic risk factors.

Statistical analysis

SAS statistical software Version 8.1 was used for all statistical analysis (SAS Institute, Cary, NC). Quartile categories of Mg intake were created and the lowest quartile category formed the referent group. Logistic regression analysis was used to examine the association between quartile categories of Mg intake, prevalence of MS and components of the MS. Models were adjusted for age, gender, BMI (except when it was outcome), race, educational attainment, marital status, smoking status, alcohol intake, exercise, energy intake (kcal), percentage of energy from saturated fat, use of antihypertensive or lipid medication. Tests for linear trends were measured across increasing quartile intake using the median value in each quartile as the intake.

Results

The study population was composed of 179 (33%) men and 356 (67%) women with an average age of 72 and 74 years for men and women, respectively. Of these, 127 (24%) participants were taking lipid lowering medication and 174 (33%) participants were taking blood pressure medication. In comparison to the study participants excluded, the final sample was more educated (47% vs. 37%, P < 0.05) and had a lower fasting glucose than those who were excluded from the analyses (mean 108.1 mg/dl vs. 129.6 mg/dl, P < 0.05). Individuals with data had significantly lower BMI (P < 0.005), although the prevalence of obesity was similar in the two groups. Individuals included in this study had significantly higher reported intake of total energy (P < 0.002) and Mg intake (P < 0.0001). There were no significant differences between the groups in prevalence of MS risk factors.

Dietary sources accounted for ~98% of total intake of magnesium and the major food contributors of Mg

included milk, coffee, orange juice, bananas and whole-wheat bread. The median daily intake of total and dietary Mg was 298 and 293 mg, respectively, in men and 251 mg and in 245 mg, respectively, in women. Between the lowest and highest quintile category of Mg intake, there was almost a 200 mg/day difference in total Mg intake. Only 14.6% of participants in the study were taking supplements, which included Mg. Older adults with the highest Mg intake were not significantly different from others with respect to age, race or in the distribution of those consuming alcohol (Table 1). However, individuals with higher Mg intakes were more likely to be male and significantly less likely to smoke, more likely to engage in regular exercising, have higher educational attainment and consumed a lower percentage of saturated fat and higher fiber intakes.

We checked for interaction between magnesium intake and metabolic risk factors by sex, age (< and \ge than 70 years) and BMI (< and ≥25) but these interactions were not statistically significant. The overall prevalence of the MS in this population was 40%. Mg intake was inversely associated with the MS; those with the highest intake of Mg had significantly lower risk of having MS compared to the lowest quartile of intake (OR: 0.36, 95% CI 0.19-0.69, P for trend 0.002) (Table 2). In addition, Mg intake was inversely related to individual components of the MS. Significant inverse relationships (P trend) were observed between Mg intake and BMI (OR: 0.47, 95% CI: 0.22-1.00, P trend = 0.03), and fasting glucose (OR: 0.41, 95% CI 0.22-0.77, P trend = 0.005). No statistical significant trends were observed between Mg intake, blood pressure, HDL cholesterol or triglycerides.

Because we previously reported an inverse association between whole-grain intake and MS in this sample of elderly, we adjusted for whole-grain intake to determine the influence of this dietary source of Mg on prevalence of MS. After adjustment for whole-grain intake, the inverse association between Mg and the MS remained statistically significant (OR 0.46, CI, 0.22–0.93, *P* trend < 0.03). We also analyzed the data using only dietary Mg intake and the inverse associations remained with MS and its components.

Discussion

In this cohort of healthy older men and women, we found a significant inverse association between Mg intake and prevalence of the MS, an observation consistent with results from studies in other populations [10, 11, 28]. One prospective study conducted in young adults (18–30 y) found that higher Mg intake was associated with a 31% lower risk of developing

Table 1 Characteristics of subjects by quartile of total magnesium intake^a

Characteristics	Quartile of magne	P for trend ^b			
	Q1 (lowest)	Q2	Q3	Q4 (highest)	
Total magnesium intake					
(n)	133	135	133	134	
Median magnesium intake (mg) ^c	188	240	298	384	0.001
Quartile range (mg)	≤215.0	215.1-265.5	265.6-332.4	>332.4	
Age (years)	73.5 ± 7.0	72.6 ± 7.9	72.9 ± 7.3	71.7 ± 7.7	0.08
Females (%)	80	75	59	52	0.001
Race (white, %)	92	95	98	96	0.08
Education (≤high school, %)	55	64	47	45	0.02
% Dyslipidemia medication	26.3	30.0	27.8	17.9	0.22
% Hypertension medication	33.1	38.5	32.3	26.1	0.13
BMI (kg/m ²)	26.3 ± 4.5	27.2 ± 4.5	26.3 ± 5.5	25.1 ± 4.0	0.008
Smokers (%)	17	18	14	8	0.02
Alcohol drinkers (%) ^d	33	39	59	41	0.06
Regular exercise (%) ^e	35	31	48	51	0.001
Total energy intake (kcal) ^f	1436 ± 380	1624 ± 375	1792 ± 364	2029 ± 363	0.001
Saturated fat (% of energy) ^c	12.3 ± 3.6	12.3 ± 3.3	11.8 ± 3.2	11.5 ± 3.4	0.001
Metabolic syndrome (%) ^g	50	45	36	28	0.001

^aValues are mean ± SD, unless otherwise specified

Table 2 Relationship between total Mg intake, metabolic risk factors, and prevalence of the metabolic syndrome and its components

Variables	Quartile of Mg intake ^a				
	Q1 (n = 133) Lowest	Q2 (n = 135)	Q3 (n = 133)	Q4 (n = 134) highest	
Median Mg intake (mg/day)	188.4	240.0	297.5	384.0	0.001
Quartile range (mg/day)	≤215.0	215.1-265.5	265.6-332.4	>332.4	
Overweight BMI $\geq 31 \text{ kg/m}^2$ for men and $\geq 27 \text{ kg/m}^2$ for women	1.00	1.30 (0.74–2.30)	0.86 (0.44–1.65)	0.47 (0.22–1.00)	0.03
Glucose (≥100 mg/dl)	1.00	0.84 (0.50-1.43)	0.83 (0.47-1.47)	0.41 (0.22-0.77)	0.005
HDL cholesterol (<40 for men or <50 mg/dl for women)	1.00	0.94 (0.56-1.57)	0.84 (0.47-1.47)	0.82 (0.44-1.53)	0.50
Elevated triglycerides (≥150 mg/dl)	1.00	0.92 (0.51-1.65)	0.73 (0.38-1.41)	0.69 (0.34-1.44)	0.28
Elevated blood pressure (≥130/85 mmHg or taking BP medication)	1.00	0.45 (0.21–0.96)	0.67 (0.29–1.55)	0.44 (0.18–1.04)	0.16
Metabolic syndrome ^c OR (95%CI)	1.00	0.74 (0.45,1.24)	0.55 (0.32,0.97)	0.36 (0.19,0.69)	0.002

^aAll model are adjusted for age, gender, race (white or other), educational attainment (grade school or less, high school, or college/graduate school), marital status (married, widowed, separated, divorced, single), smoking (current or former/never smoker), alcohol intake, exercise (at least 3 times per week or less), BMI, total energy intake, percentage energy of saturated fatty acid intake, lipid lowering medication use (yes or no), and blood pressure medication (yes or no), except for the model with blood pressure as the outcome

MS over 15 years of follow-up [11]. In the Women's Health Study, a cohort of women 45 years or older, higher Mg intake was associated with a 27% lower risk of having MS [28]. With respect to individual components of the MS, low Mg intake appears to be linked

to greater dyslipdemia [3, 11] and hypertension [3, 11, 15, 23]. In this sample of community-living older individuals, however, we observed no relationship between dietary Mg intake and either dyslipidemia or hypertension. This may be due in part to the different

^bP for trend test for continuous variable used the median value in each quartile as a continuous variable in linear regression; for categorical variable used Mantel–Haenszel chi-square

^cControlled for calorie intake, age and sex

dAt least 1-2 drinks/week

^ePhysical exercise at least three times a week

^fControlled for age and sex

gMetabolic syndrome is defined in this study as having 3 of the following 5 criteria: HDL < 40 mg/dl for men or <50 mg/dl for women, fasting glucose ≥100 mg/dl, triglyceride ≥150 mg/dl, blood pressure ≥130/85 mmHg or being on BP medication, and BMl ≥ 31 kg/m² for men or ≥27 kg/m² for women

^bTests for linear trends were measured across increasing quartile intake using the median value in each quartile as the intake

Logistic regression models were used to examine the association between MS and its components and Mg intake. MS is defined in this study as having 3 of the following 5 criteria: HDL <40 mg/dl for men or <50 mg/dl for women, fasting glucose \geq 100 mg/dl, triglyceride \geq 150 mg/dl, blood pressure \geq 130/85 mmHg or being on BP medication, and BMI \geq 31 kg/m² for men or \geq 27 kg/m² for women. The cutoff of the metabolic risk factors were based on ATPIII criteria for each component. Data are odds ratio (OR) (95% confidence intervals, 95% CI)

age group of this population compared to other cohorts with younger participants [3, 11].

The two components of the MS most strongly associated with Mg intake in our population were fasting glucose concentrations and BMI. Experimental studies have shown improvements in insulin sensitivity and glucose control among individuals with type 2 DM [16, 18, 29] and healthy older adults (>70 years) receiving magnesium supplements [17]. One clinical randomized trial found that among individuals with type 2 diabetes who had low serum Mg concentrations, fasting plasma glucose concentrations were significantly reduced (37.5%) following oral Mg supplementation for 16 weeks [20]. In another study, insulin-mediated glucose disposal was worse in healthy patients free of diabetes with low compared to high Mg status [21], suggestive that Mg status affects insulin and glucose metabolism. Further evidence that Mg plays a role in glucose metabolism arises from a meta-analysis of several randomized, double-blind, placebo-controlled trials in which oral Mg supplementation for 4-16 weeks was effective in reducing plasma glucose levels in patients with type 2 diabetes [26]. In our study of older adults, we found that those with the highest intake of Mg had the lowest prevalence of fasting hyperglycemia. In a study conducted in healthy young adults [11], the prevalence of fasting hyperglycemia was approximately half in the lowest compared to the highest quartile of magnesium intake. Because Mg acts as a cofactor for a number of glucose relevant enzymes, a low Mg status may directly affect the regulation of glucose metabolism via its effect on enzymatic function [24].

In the present study, men and women with the highest Mg intake were less likely to be overweight/ obese than those with the lowest intakes. Using waist circumference to define abdominal adiposity using the ATP III criteria [5], a higher Mg was associated with a lower prevalence of abdominal adiposity or central obesity in young adults (18-30 years) [11] and in adults between the ages of 45 and 64 years [3]. In type 2 DM patients, low magnesium status was associated with greater abdominal adiposity, as defined by waist-circumference [4]. Unfortunately, waist circumference measures were not available in this study to capture abdominal adiposity, and although we applied corresponding waist circumference thresholds in a representative population to derive a BMI cut-point [30], we may have underestimated the number of people with abdominal adiposity. Currently, the scientific evidence that Mg is directly involved in body weight regulation is lacking. However, even after accounting for energy intake and physical activity, the inverse relation between magnesium intake and overweight persisted. Because Mg is found in a wide range of foods including whole grains, green leafy vegetables, nuts, legumes and dairy products, it may be the overall dietary pattern, not magnesium intake per se, that contributes to lower BMI. Alternatively, energy intake and physical activity may not have been accurately captured, and consequently not appropriately controlled in this study, resulting in residual confounding. However, a recognized limitation of all observational studies is the difficulty in establishing an independent effect from a single nutrient, versus the combined effects of nutrients in foods and/or dietary patterns.

As with all cross-sectional study designs, we cannot draw any conclusions regarding the temporal relation between exposure and outcome, and such temporal relations can only be derived from prospective studies. However, this study generates a further hypothesis that can be tested in other populations, specifically, a high Mg intake prevents the progression of MS, i.e., a worsening of metabolic risk factors. Also, we cannot conclude that these observed protective associations with higher Mg intake are not due to the possibility of residual confounding or confounding by other healthy lifestyle characteristics. Notably, we did attempt to adjust for some of the stronger lifestyle risk factors, such as engaging in regular exercise, smoking and BMI. We previously reported that higher intake of whole-grains was related to a lower prevalence of the MS in this cohort of older adults [23]. However, magnesium is found in many other foods, and an independent association was observed between Mg and MS, albeit weaker, after adjusting for whole grain intakes. Finally, these participants were self-selected and so are not representative of older people in the population, thereby limiting the generalizability of these findings to other populations.

The strengths of this study include the relatively large number of adults over 70 years of age for whom we had dietary, anthropometric and clinical data. Also, diet records were used to estimate dietary Mg intake as opposed to 24-h recalls or questionnaires which use fixed food categories. Older adults may have difficulty recalling dietary intake over the previous 6–12 months as instructed in most questionnaires, and while diet records are not devoid of recording bias, participants were instructed on how to complete the diary by a trained dietitian who later reviewed each record with the participants.

In the EPIC-Postdam study [25], there was no relationship between dietary magnesium intake and type 2 DM risk, but there was a protective association with cereal fiber intake (predominantly from wholegrains). As mentioned earlier, whole-grains are an important source of cereal fiber and dietary magnesium. A limitation of observational studies is that it can be difficult to separate the effects of nutrients from those of foods. Confirmation of the independent

roles of dietary magnesium and cereal fiber in MS and type 2 DM risk may need to await large-scale, magnesium supplementation intervention trials.

In conclusion, we found that Mg intake was inversely associated with the prevalence of MS in older adults. This study highlights the importance for older adults to consume food sources rich in Mg, such as whole-grains, legumes and green leafy

vegetables. Based on the modified food guide pyramid for people over 70 years of age, these foods can be eaten by most people in this age group if properly prepared: cooked, grated or chopped [22]. Furthermore, it emphasizes the need for an intervention study designed to test the independent effect of magnesium on changes of metabolic risk factors, particularly pre-diabetic risk factors.

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